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ETIOLOGY OF ASYMPTOMATIC MICROSCOPIC HEMATURIA IN ADULTS

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Asymptomatic microscopic hematuria is a common finding that demands urologic evaluation. Of the 236 patients over the age of 40, 6.8% were found to have a genitourinary cancer, while 27.5% had other significant urologic disease. However, 52.1% of the patients had unknown etiology of microscopic hematuria and 13.6% had insignificant urologic lesions. Of the 72 patients under the age of 40 a positive diagnosis was made in 16 patients (22.2%). Cystoscopic examination was of diagnostic value in only 1 patient. Therefore, cystoscopy is of little diagnostic value in young patients. Once asymptomatic microscopic hematuria is established and no etiological cause is identified, we follow the patient by urinalysis and cytology every three months and reevaluate the patient in whom urological symptoms develop.

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Key words: Microscopic hematuria, Urologic disease, Genitourinary cancer

INTRODUCTION

Asymptomatic microscopic hematuria in adults frequently proposes a diagnostic dilemma and management problem for the practicing urologist. It is one of the most common enigma requiring urological investigation. The evaluation and treatment of patients with microscopic hematuria in reported series have revealed that 4.8% to 16.5% of the patients have serious urologic diseases[1-4]. The etiology of hematuria may range from conditions posing minimal risk to the patient, such as cystitis, to potentially life-threatening conditions, such as malignancy[1-3]. The urologist must differentiate the early potentially curable malignancies that may present with hematuria from the more benign conditions that may also cause hematuria. The specific problem is to diagnose these serious conditions while minimizing the cost and morbidity associated with the diagnostic procedure. We have evaluated 236 patients who were referred for urologic work up for microsopic hematuria by renal ultrasound, intravenous urography (IVU), urinary cytology and cystoscopy. The incidence of urological neoplasms and other significant genitourinary lesions was compared to a previous large series on microscopic hematuria[1-4].

MATERIAL AND METHODS

We have reviewed the charts of 308 pateints who had been referred for urologic evaluation for microscopic hematuria from January 1991 to December 1992. These patients were asymptomatic and were referred because of microscopic hematuria detected on routine examination. The presence of microscopic hematuria was confirmed by greater than 3 red blood cells/high power field on two out of three properly collected clean catch urine specimens. Those patients with proteinuria and casts were excluded. However, patients with pyuria and/or bacteriuria were included because of frequent coincidence of tumors or stones with urinary infections. The patients of this series were subdivided into two groups. One group (236 patients) was over 40 years old (105 men and 131 women), with an average age of 52.6 years. The other group (72 patients) was under 40 years old (52 men and 20 women), with an average age of 34.6 years. They were evaluated by repeated urinalysis, urinary cytology, renal ultrasound, IVU and cystoscopy. Diagnosis by the aforementioned examinations was classified by the methods of Green and associates[1]. Highly significant lesions were likely to be fatal without prompt treatment. In moder-

ately significant lesions hematuria could be expected to resolve with treatment but immediate treatment was unnecessary, since there was no threat to life. Insignificant lesions were those in which it was unclear whether they actually caused the hematuria.

RESULTS

Of the 236 cases of patients over 40 years old 102 had urologic diseases that could be etiology for microscopic hematuria on initial evaluation. In one male patient, gross hematuria developed due to bladder cancer one year after negative initial evaluation. Colic pain secondary to ureteral calculi developed in 2 patients 4 months and 7 months following a negative X-ray examination, ultrasound, cytology and cystoscopic examination. Six and two patients were found to have glomerulonephritis and IgA nephropathy, respectively. They were initially unexplained. Therefore, 113 patients (47.9%) had urologic abnormalities determined. Of the 113 patients with established etiology of the microscopic hematuria, 16 had highly significant lesions, 65 had moderately significant lesions, 32 had insignificant lesions, and 123 had undetermined causes (Table 1). There were 8 patients with genitourinary malignancy: 5 patients had bladder tumor, 1 renal cell carcinoma, 1 prostate cancer, and 1 renal pelvic cancer. There were 6 cases of biopsy-proved glomerulonephritis and 2 cases of IgA nephropathy. The moderately significant lesions group included 28 patients with bacterial cystitis, 17 cases of renal stone, 8 cases of ureteral stone, 7 cases of cystitis cystica, 2 cases of radiation cystitis, 2 cases of ureteropelvic junction obstruction, and 1 case of

Table 1. Lesions found with evaluation of asymptomatic microscopic hematuria in the patients over the age of 40.

	Men	Women	Totals
Highly significant lesions:			
Bladder Cancer	4	1	5
Renal Cancer	1		1
Prostatic Cancer	1		1
Renal pelvic Cancer		1	1
Chronic Glomerulonephritis	2	2	4
Focal Glomerulonephritis	1	1	2
IgA Nephropathy		2	2
Total No. (%)	9 (8.6)	7 (5.3)	16 (6.8)
Moderately significant lesions:			
Bacterial Cystitis		28	28
Urolithiasis	15	10	25
Cystitis Cystica		7	7
Radiation Cystitis		2	2
Ureteropelvic Junction Obstruction	2		2
Polycystic Kidney		1	1
Total No. (%)	17 (16.2)	48 (36.6)	65 (27.5)
Insignificant lesions:			
Renal Cyst	9	5	14
Urethral Caruncle		13	13
Bladder Diverticulum	2	2	4
Ureteral duplication		1	1
Total No. (%)	11 (10.5)	21 (16)	32 (13.6)
N. unexplained (%)	68 (65)	55 (42)	123 (52.1)
Total No. (%)	105 (100)	131 (100)	236 (100)

polycystic kidney. The insignificant lesions group contained 14 patients with renal cyst, 13 patients with urethral caruncle, 4 patients with bladder diverticulum, and 1 patient with ureteral duplication. For the most part this group represented incidental urologic abnormalities that were difficult to implicate as the cause for microscopic hematuria.

Of the 72 patients under 40 years old there were positive findings in 16 patients (23%) (Table 2). Six patients were found to have tender prostate on rectal examination. Four female patients had bacterial cystitis. Four patients admitted to taking frequent sterenuous exercise. They were asked to refrain from exercise for 1 week and their urine was retested. All 4 had resolution of their hematuria. One patient had papillary bladder tumor and 1 patient had renal stone.

Table 2. Positive findings in 16 patients under the age of 40 with microscopic hematuria.

	Men	Women	Totals
Prostatitis	6		6
Bacterial Cystitis		4	4
Exercise hematuria	2	2	4
Bladder Cancer	1		1
Urolithiasis	1		1
Total	10	6	16

DISCUSSION

Significant hematuria is difficult to define for three reasons; normal individuals excrete erythrocytes in their urine; urinalysis results are very dependent upon collection and storage methods and urinalysis technique; and, hematuria is often intermittent. Larcom and Carter noted that normal urinary erythrocyte excretion would correspond to 2 RBC/HPF on a standard urinalysis sediment count[5]. For 5,000 men and 1,000 women being screened for insurance physicals the 95% confidence levels were 1 to 2 RBC/HPF for men and 4 to 5 RBC/HPF for women[6]. It is our policy to evaluate all patients with greater than 3 RBC/HPF on two out of three properly collected clean catch urine specimens. Among the patients over the age of 40, men were more likely to have serious urologic diseases (6 of 8 cases of malignancy in our series were men). Women were more likely to have inflammatory diseases. As would be expected, older patients were more likely to have serious underlying pathology.

According to Green et al., there were 11 patients (2.2%) with genitourinary malignancies in a series of 500 patients. Since then, there have been two other large series dealing with the same subject. In 1979 Carson, Segura and Greene[2] reported a 12.5% incidence of malignancy in a series of 200 patients, whereas Golin and Howard in 1980[3] reported a 10% incidence of malignancy in a series of 247 patients. In our series, the incidence of genitourinary malignancy was 6.8%. The incidence of urolithiasis was 5.6% in Greene's series, 16.5% in Carson's series, 3.5% in Golin's series and 10.6% in our serias.

Renal parenchymal disease (that is excluding primary renal neoplasms) as a cause of microhematuria has an unknown incidence. These patients often may be referred for urologic evaluation without numerous red cell casts and heavy proteinuria, which would immediately suggest glomerular disease. The cause was initially considered unknown in all our patients with biopsy-proved glomerulonephritis. None of our patients with glomerulonephritis had an abnormal nephritis profile. Focal glomerulonephritis, which may be idiopathic or seen as the result of other conditions such as systemic lupus erythematosus or polyarteritis nodosa, can present with hematuria and minimal proteinuria. An IgA nephropathy, in which hematuria precedes the often associated upper respiratory tract infection and renal involvement with other systemic disorders, such as lymphoma, myeloma or amyloidosis are possible etiologies for unexplained hematuria.

Of the 16 young patients in this study with a positive finding after full investigation, cystoscopic detection of urologic disease was made in only 1 male patient. He was thirty five years old and had bladder

cancer with positive urinary cytology. Murakami et al. reported that the positive rate of ultrasound in the diagnosis of bladder cancer was as low as 15.4%[7]. However, the detection rate of urinary cytology is relatively high at 54%[7]. They asserted that it might be reasonable to use cystoscopy in patients younger than 40 years when cytology studies are positive. Jones et al. performed a prospective study of 100 young men under the age of 40 with microscopic hematuria and concluded that cystoscopy is of minimal diagnostic value in young men[8]. Our findings suggest that cystoscopic examination should be reserved for those patients in whom non-invasive examinations indicate the presence of treatable cause of hematuria in the lower urinary tract.

Golin and Howard[3], in their protocol of follow-up of cases of microhematuria without firm diagnosis, recommended urinalysis and a cytology examination every six months and intravenous pyelography and cystoscopy alternating biannually. Recently, they changed their followup protocol based on their reassessment of their 10 to 20 year followup of 191 patients with unexplained microscopic hematuria[9]. They reviewed the charts of 191 patients 10 to 20 years after the initial evaluation for asymptomatic microhematuria. Genitourinary malignancies did not develop in any of the patients. Therefore, they have abandoned routine periodic studies and advise diagnostic studies only for patients in whom symptoms develop. However, this strategy should be scrutinized in other study series.

Our followup protocol for asymptomatic microscopic hematuria is as follows. Once asymptomatic microhematuria is established and complete urological evaluation is negative, then the patients are instructed to return for evaluation every three months for urinalysis and urine cytology. The interval is determined by the risk status of the patient. Patients are instructed to return when they experience irritative voiding symptoms or gross hematuria. Hematuria is a significant finding and as defined, it warrants complete urologic investigation. In the patients under 40 years cystoscopy may be unhelpful and is of value only when simple examinations suggest that a significant lesion exists in the lower urinary tract.

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和文抄録

成人における無症候性顕微鏡的血尿の原因

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無症候性顕微鏡的血尿は，泌尿器科的精査を要するありふれた症状である．精査を行った40歳以上の患者群236例のうち，6.8%に尿路性器癌が発見された．27.5%に重篤な泌尿器疾患が見いだされた．52.1%の症例においては，顕微鏡的血尿の原因が不明であった．13.6%の症例において，重篤ではない泌尿器疾患が見いだされた．一方，40歳以下の群では，72例中16例（22.2%）に異常所見が認められた．これらのうち，膀胱鏡検査により疾患が発見されたのは，わずかに1例であった．従って若年者に対する膀胱鏡検査はほとんど価値がないと考えられる．無症候性顕微鏡的血尿に対し，泌尿器科的精査を行い，明らかな基礎疾患が見いだされなかった場合は，三カ月ごとに尿検査と尿細胞診を行うことによってフォローし，症状が出現してくるようであれば，再精査をすることを原則としている．

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